

IN THE CLAIMS:**Replace claims 1-3, 8-11, 15-19, 23, 25, 27, 28, 30, 32, and 33 as originally filed with****amended claims 1-3, 8-11, 15-19, 23, 25, 27, 28, 30, 32, and 33.****Cancel claims 24 and 34-40.****RECEIVED**

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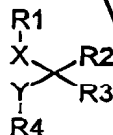
1. (Amended) A pharmaceutical formulation, comprising:

(i) an inhibitor of carboxypeptidase U or a pharmaceutically acceptable salt thereof; and

(ii) a thrombin inhibitor or a derivative thereof,

in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier.

2. (Amended) The pharmaceutical formulation according to claim 1, wherein the inhibitor of carboxypeptidase U is a compound of general formula I



or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, wherein:

 R_1 is selected from the group consisting of:C₁-C₆ alkyl, substituted with one or more basic groups;

cycloalkyl, substituted with one or more basic groups;

heterocyclyl, comprising at least one nitrogen atom;

heterocyclyl, comprising at least one hetero atom selected from S or O, and substituted with one or more basic groups; and

aryl, substituted with one or more basic groups;

 R_2 is selected from the group consisting of H, acyl, acylamino, alkyl, alkylcarbamoyl, alkylthio, alkoxy, aroyl, aroylamino, aryloxy, arylthio, amidino, amino, aryl, carbamoyl, carboxy, cyano, cycloalkyl, formyl, guanidino, halogen, heterocyclyl, hydroxy, oxo, nitro, thiol, Z₂N-CO-O-, ZO-CO-NZ-, and Z₂N-CO-NZ-;

R_3 is selected from the group consisting of COOR_5 , $\text{SO}(\text{OR}_5)$, SO_3R_5 , $\text{P}=\text{O}(\text{OR}_5)_2$, $\text{B}(\text{OR}_5)_2$, $\text{P}=\text{OR}_5(\text{OR}_5)$, tetrazole, and a carboxylic acid isostere;

R_4 is SH , $\text{S-CO-C}_1\text{-C}_6$ alkyl, or S-CO-aryl ;

R_5 is H , $\text{C}_1\text{-C}_6$ alkyl, or aryl;

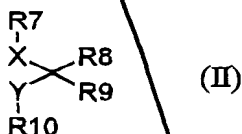
R_6 is H or $\text{C}_1\text{-C}_6$ alkyl;

X is selected from the group consisting of O , S , SO , SO_2 , $\text{C}(\text{Z})_2$, $\text{N}(\text{Z})$, NR_6SO_2 , SO_2NR_6 , NR_6CO , and CONR_6 ;

Y is $\text{C}(\text{Z})_2$; and

Z is independently selected from the group consisting of H , $\text{C}_1\text{-C}_6$ alkyl, aryl, cycloalkyl and heterocyclyl.

3. (Amended) The pharmaceutical formulation according to claim 1, wherein the inhibitor of carboxypeptidase U is a compound of general formula II,



or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, wherein:

R_7 is selected from the group consisting of:

$\text{C}_1\text{-C}_6$ alkyl, substituted with one or more basic groups;

cycloalkyl, substituted with one or more basic groups;

heterocyclyl, comprising at least one nitrogen atom;

heterocyclyl, comprising at least one hetero atom selected from S or O ,

and substituted with one or more basic groups; and

aryl, substituted with one or more basic groups;

R_8 is selected from the group consisting of H , acyl, acylamino, alkyl, alkylcarbamoyl, alkylthio, alkoxy, aroyl, aroylamino, aryloxy, arylthio, amidino, amino, aryl, carbamoyl, carboxy, cyano, cycloalkyl, formyl, guanidino, halogen, heterocyclyl, hydroxy, oxo, nitro, thiol, $\text{Z}_2\text{N-CO-O-}$, ZO-CO-NZ- , and $\text{Z}_2\text{N-CO-NZ-}$;

R_9 is selected from the group consisting of COOR_{11} , $\text{SO}(\text{OR}_{11})$, SO_3R_{11} , $\text{P}=\text{O}(\text{OR}_{11})_2$, $\text{B}(\text{OR}_{11})_2$, $\text{P}=\text{OR}_{11}(\text{OR}_{11})$, tetrazole, and a carboxylic acid isostere;

R_{10} is a $\text{—}\overset{\text{O}}{\overset{\text{R}_{11}}{\text{P}}}\text{—R}_{12}$ -group, a $\text{—}\overset{\text{O}}{\text{C}}\text{—N}(\text{R}_{13})\text{—OH}$ -group, or a $\text{—}\overset{\text{O}}{\text{C}}\text{—R}_{11}$ -group;

R_{11} is H, $\text{C}_1\text{—C}_6$ alkyl, or aryl;

R_{12} is $\text{C}_1\text{—C}_6$ alkyl, aryl, cycloalkyl, heterocyclyl, or an optionally N-substituted

$\text{H}_2\text{N—C(Z)—CONH—C(Z)—}$ or $\text{H}_2\text{N—C(Z)—}$ group;

R_{13} is H or $\text{C}_1\text{—C}_6$ alkyl;

X is selected from the group consisting of O, S, SO, SO_2 , C(Z)_2 , N(Z) , $\text{NR}_{13}\text{SO}_2$, $\text{SO}_2\text{NR}_{13}$, NR_{13}CO , and CONR_{13} ;

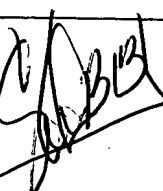
Y is selected from the group consisting of O, N(Z) , S, C(Z)_2 , and a single bond; and

Z is independently selected from the group consisting of H, $\text{C}_1\text{—C}_6$ alkyl, aryl, cycloalkyl, and heterocyclyl,

with the proviso that when X is O, S, SO, SO_2 , N(Z) , NR_7SO_2 , SO_2NR_7 , or NR_7CO , then Y is C(Z)_2 or a single bond.

4. (Not amended herein) The pharmaceutical formulation according to any previous claim, wherein the thrombin inhibitor is a low molecular weight thrombin inhibitor.
5. (Not amended herein) The pharmaceutical formulation according to claim 4, wherein the low molecular weight thrombin inhibitor is a peptide-based, amino acid-based, and/or peptide analogue-based, thrombin inhibitor with one to four peptide linkages.
6. (Not amended herein) The pharmaceutical formulation according to claim 5, wherein the low molecular weight thrombin inhibitor is $\text{HOOC—CH}_2\text{—(R)Cgl—Aze—Pab—H}$ or a prodrug thereof.

7. (Not amended herein) The pharmaceutical formulation according to claim 6, wherein the prodrug is $\text{EtOOC-CH}_2\text{-(R)Cgl-Aze-Pab-OH}$.

 8. (Amended) The pharmaceutical formulation according to any one of claims 1-3, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 1000:1 to about 1:1000.

9. (Amended) A kit of parts comprising:

- (i) a vessel comprising an inhibitor of carboxypeptidase U, or a pharmaceutically acceptable salt thereof;
- (ii) a vessel comprising a thrombin inhibitor, or a derivative thereof; and
- (iii) instructions for the sequential, separate or simultaneous administration of the inhibitors (i) and (ii) to a patient in need thereof.

A² 10. (Amended) A kit of parts comprising:

- (i) a vessel comprising an inhibitor of carboxypeptidase U, or a pharmaceutically acceptable salt thereof;
 - (ii) a vessel comprising a thrombin inhibitor, or a derivative thereof; and
 - (iii) instructions for the sequential, separate, or simultaneous administration of the inhibitors (i) and (ii) to a patient in need thereof;
- wherein the inhibitor of carboxypeptidase U is a compound according to claim 2 or 3.

11. (Amended) The kit of parts according to claim 9, wherein the thrombin inhibitor is a low molecular weight thrombin inhibitor.

12. (Not amended herein) The kit of parts according to claim 11, wherein the low molecular weight thrombin inhibitor is a peptide-based, amino acid-based, and/or peptide analogue-based, thrombin inhibitor with one to four peptide linkages.

13. (Not amended herein) The kit of parts according to claim 12, wherein the low molecular weight thrombin inhibitor is $\text{HOOC-CH}_2\text{-(R)Cgl-Aze-Pab-H}$ or a prodrug thereof.

14. (Not amended herein) The kit of parts according to claim 13, wherein the prodrug is $\text{EtOOC-CH}_2\text{-(R)Cgl-Aze-Pab-OH}$.

15. (Amended) The kit of parts according to claim 9, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 1000:1 to about 1:1000.

16. (Amended) A kit of parts comprising:

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- (i) a pharmaceutical formulation comprising an inhibitor of carboxypeptidase U, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier; and
 - (ii) a pharmaceutical formulation comprising a thrombin inhibitor, or a derivative thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier,
- wherein inhibitors (i) and (ii) are each formulated for administration in conjunction with the other.

17. (Amended) The kit of parts according to claim 16, wherein inhibitors (i) and (ii) are formulated for sequential, separate or simultaneous administration.

18. (Amended) A kit of parts comprising:

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- (i) a pharmaceutical formulation comprising an inhibitor of carboxypeptidase U, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier; and
 - (ii) a pharmaceutical formulation comprising a thrombin inhibitor, or a derivative thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier,
- wherein inhibitors (i) and (ii) are each formulated for administration in conjunction with the other, and
- wherein the inhibitor of carboxypeptidase U is a compound according to claim 2 or 3.

A3 19. (Amended) The kit of parts according to claim 16 or 17, wherein the thrombin inhibitor is a low molecular weight thrombin inhibitor.

20. (Not amended herein) The kit of parts according to claim 19, wherein the low molecular weight thrombin inhibitor is a peptide-based, amino acid-based, and/or peptide analogue-based, thrombin inhibitor with one to four peptide linkages.

21. (Not amended herein) The kit of parts according to claim 20, wherein the low molecular weight thrombin inhibitor is $\text{HOOC-CH}_2\text{-(R)Cgl-Aze-Pab-H}$ or a prodrug thereof.

22. (Not amended herein) The kit of parts according to claim 21, wherein the prodrug is $\text{EtOOC-CH}_2\text{-(R)Cgl-Aze-Pab-OH}$.

A4 23. (Amended) The kit of parts according to claim 16, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 1000:1 to about 1:1000.

25. (Amended) A method for the treatment of a patient suffering from, or susceptible to, a condition in which inhibition of thrombin and/or inhibition of carboxypeptidase U are required or desired, which method comprises administering to the patient a therapeutically effective total amount of:

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- (i) an inhibitor of carboxypeptidase U, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier; and
 - (ii) a thrombin inhibitor, or a derivative thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier.

26. (Amended) The method according to claim 25, wherein the administration of inhibitors (i) and (ii) is sequential, separate or simultaneous.

27. (Amended) A method for the treatment of a patient suffering from, or susceptible to, a condition in which inhibition of thrombin and/or carboxypeptidase U are required or desired, which method comprises administering to the patient a therapeutically effective total amount of:

- (i) an inhibitor of carboxypeptidase U, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier; and
- (ii) a thrombin inhibitor, or a derivative thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier,

wherein the inhibitor of carboxypeptidase U is a compound according to claim 2 or 3.

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28. (Amended) The method according to ~~any one of claims 25 or 26~~, wherein the thrombin inhibitor is a low molecular weight thrombin inhibitor.

29. (Amended) The method according to claim 28, wherein the low molecular weight thrombin inhibitor is a peptide-based, amino acid-based, and/or peptide analogue-based, thrombin inhibitor with one to four peptide linkages.

30. (Amended) The method according to claim 29, wherein the low molecular weight thrombin inhibitor is HOOC-CH₂-(R)Cgl-Aze-Pab-H or a prodrug thereof.

31. (Not amended herein) The method according to claim 30, wherein the prodrug is EtOOC-CH₂-(R)Cgl-Aze-Pab-OH.

32. (Amended) The method according to claim 25 or 26, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 1000:1 to about 1:1000.

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33. (Amended) A method for treatment of a patient suffering from, or susceptible to, a condition in which inhibition of thrombin and/or inhibition of carboxypeptidase U are required or desired,

AG which method comprises administering to the patient a formulation according to any one of claims 1 to 3.

Add new claims 41-63.

41. (New) The pharmaceutical formulation according to any one of claims 2 or 3, wherein the basic group is selected from the group consisting of amino, amidino, and guanidino.
42. (New) The pharmaceutical formulation according to any one of claims 1-3, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 50:1 to about 1:50.
43. (New) The kit of parts according to claim 10, wherein the thrombin inhibitor is a low molecular weight thrombin inhibitor.
44. (New) The kit of parts according to claim 43, wherein the low molecular weight thrombin inhibitor is a peptide-based, amino acid-based, and/or peptide analogue-based, thrombin inhibitor with one to four peptide linkages.
45. (New) The kit of parts according to claim 44, wherein the new low molecular weight thrombin inhibitor is $\text{HOOC-CH}_2\text{-(R)Cgl-Aze-Pab-H}$ or a prodrug thereof.
46. (New) The kit of parts according to claim 45, wherein the prodrug is $\text{EtOOC-CH}_2\text{-(R)Cgl-Aze-Pab-OH}$.
47. (New) The kit of parts according to claim 9, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range from about 50:1 to 1:50.
48. (New) The kit of parts according to claim 10, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range from about 1,000:1 to about 1:1,000.
49. (New) The kit of parts according to claim 10, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range from about 50:1 to 1:50.

50. (New) The kit of parts according to claim 18, wherein the thrombin inhibitor is a low molecular weight thrombin inhibitor.
51. (New) The kit of parts according to claim 50, wherein the low molecular weight thrombin inhibitor is a peptide-based, amino acid-based, and/or peptide analogue-based, thrombin inhibitor with one to four peptide linkages.
52. (New) The kit of parts according to claim 51, wherein the low molecular weight thrombin inhibitor is $\text{HOOC-CH}_2\text{-(R)Cgl-Azc-Pab-H}$ or a prodrug thereof.
53. (New) The kit of parts according to claim 52, wherein the prodrug is $\text{EtOOC-CH}_2\text{-(R)Cgl-Aze-Pab-OH}$.
54. (New) The kit of parts according to claim 16, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 50:1 to about 1:50.
55. (New) The kit of parts according to claim 18, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 1,000:1 to about 1:1,000.
56. (New) The kit of parts according to claim 18, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 50:1 to about 1:50.
57. (New) The method according to claim 27, wherein the thrombin inhibitor is a low molecular weight thrombin inhibitor.
58. (New) The method according to claim 57, wherein the low molecular weight thrombin inhibitor is a peptide-based, amino acid-based, and/or peptide analogue-based, thrombin inhibitor with one to four peptide linkages.
59. (New) The method according to claim 58, wherein the low molecular weight thrombin inhibitor is $\text{HOOC-CH}_2\text{-(R)Cgl-Aze-Pab-H}$ or a prodrug thereof.

60. (New) The method according to claim 59, wherein the prodrug is EtOOC-CH₂-(R)Cgl-Aze-Pab-OH.
61. (New) The method according to claim 25, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 50:1 to about 1:50.
62. (New) The method according to claim 27, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 1,000:1 to about 1:1,000.
63. (New) The method according to claim 27, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 50:1 to about 1:50.
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